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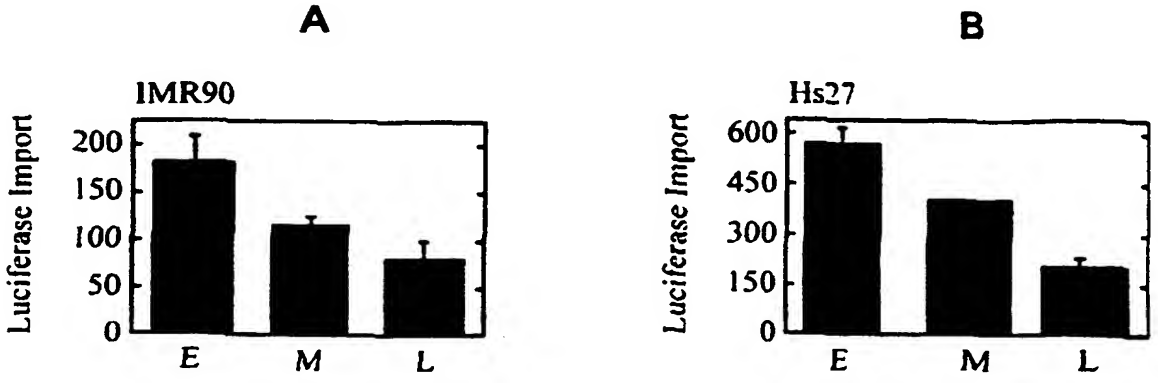
(54) Title: PROMOTION OF PEROXISOMAL CATALASE FUNCTION IN CELLS



(57) Abstract: The molecular mechanisms of peroxisome biogenesis have begun to emerge: in contrast, relatively little is known about how the organelle functions as cells age. The present inventors characterized age-related changes in peroxisomes of human cells and showed that aging compromises peroxisomal targeting signal 1 (PTS1) protein import, with the critical antioxidant enzyme, catalase, especially affected. The number and appearance of peroxisomes are altered in these cells, and the organelles accumulate the PTS1-import receptor, Pex5p, on their membranes. Concomitantly, cells produce increasing amounts of the toxic metabolite, H_2O_2, and this increased load of reactive oxygen species (ROS) may further reduce peroxisomal protein import and exacerbate the effects of aging. Disclosed are novel compositions and methods for restoring catalase in peroxisomes by use of targeted catalase modified at its C-terminus and/or N-terminus, optionally in combination with polypeptides which promote cellular uptake of proteins, to prevent or overcome the changes that follows aging or that are associated with a number of diseases or disorders.

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